

L Number	Hits	Search Text	DB	Time stamp
5	20840	HHV-8 or herpes\$10	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/06/21 17:05
12	1581	(HHV-8 or herpes\$10) and (interleukin-6 or IL-6 or V-IL-6 or vIL-6)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/06/21 17:08
18	40	(HHV-8 or herpes\$10) WITH (interleukin-6 or IL-6 or V-IL-6 or vIL-6)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/06/21 17:08
28	13	(US-5854398-\$ or US-5861500-\$ or US-5849564-\$ or US-6060284-\$ or US-6177080-\$ or US-6183751-\$ or US-6348586-\$).did. or (WO-9803657-\$ or US-5854398-\$ or US-5861500-\$).did. or (US-6183751-\$ or WO-9803657-\$ or US-6264958-\$).did.	USPAT; EPO; DERWENT	2002/06/21 17:21
-	10	((("5854398") or ("5861500") or ("5849564") or ("6183751"))).PN.	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2002/06/21 17:04

(FILE 'HOME' ENTERED AT 16:34:46 ON 21 JUN 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'  
ENTERED AT 16:35:03 ON 21 JUN 2002  
L1 19379 S HHV-8 OR (HERPES VIRUS)  
L2 377 S L1 AND (INTERLEUKIN-6 OR IL-6 OR V-IL-6 OR VIL-6)  
L3 160 DUP REM L2 (217 DUPLICATES REMOVED)  
L4 160 FOCUS L3 1-  
L5 16 S L4 AND PY<=1996  
L6 16 SORT L5 PY  
L7 248995 S HHV-8 OR HHV? OR HERPES?  
L8 1971 S L7 AND (INTERLEUKIN-6 OR IL-6 OR V-IL-6 OR VIL-6)  
L9 643 S L8 AND PY<=1996  
L10 357 DUP REM L9 (286 DUPLICATES REMOVED)  
L11 357 FOCUS L10 1-  
L12 78 S L11 AND ((HHV-8 OR HHV? OR HERPES?)(L)(INTERLEUKIN-6 OR IL-6  
L13 78 FOCUS L12 1-  
L14 1033 S FLECKENSTEIN B?/AU  
E FLECKENSTEIN B?/AU  
L15 205 S E6  
L16 7 S L15 AND L8  
L17 5 DUP REM L16 (2 DUPLICATES REMOVED)  
L18 5 SORT L17 PY

=> d an ti so au ab pi l18 1 3 4

L18 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS  
AN 1996:760040 CAPLUS  
DN 126:55664  
TI Human **herpesvirus 8** encodes a homolog of **interleukin-6**  
SO Journal of Virology (1997), 71(1), 839-842  
CODEN: JOVIAM; ISSN: 0022-538X  
AU Neipel, Frank; Albrecht, Jens-Christian; Ensser, Armin; Huang, Yao-Qi; Li, Jian Jun; Friedman-Kien, Alvin E.; **Fleckenstein, Bernhard**  
AB Kaposi's sarcoma is a multifocal lesion that is reported to be greatly influenced by cytokines such as **interleukin-6** (**IL-6**) and oncostatin M. DNA sequences of a novel human gammaherpesvirus, termed human **herpesvirus 8** (**HHV-8**) or Kaposi sarcoma-assocd. **herpesvirus**, have been identified in all epidemiol. forms of Kaposi's sarcoma with high frequency. The presence of **HHV-8** DNA is also clearly assocd. with certain B-cell lymphomas (body cavity-based lymphomas) and multicentric Castleman's disease. Sequence anal. of a 17-kb fragment revealed that adjacent to a block of conserved **herpesvirus** genes (major DNA-binding protein, glycoprotein B, and DNA polymerase), the genome of **HHV-8** encodes structural homolog of **IL-6**. This cytokine is involved not only in the pathogenesis of Kaposi's sarcoma but also in certain B-cell lymphomas and multicentric Castleman's disease. The viral counterpart of **IL-6** (**vIL-6**) has conserved important features such as cysteine residues involved in disulfide bridging or an amino-terminal signal peptide. Most notably, the region known to be involved in receptor binding is highly conserved in **vIL-6**. This conservation of essential features and the remarkable overlap between diseases assocd. with **HIV-8** and diseases assocd. with **IL-6** dysregulation clearly suggest that **vIL-6** is involved in **HHV-8** pathogenesis.

L18 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS  
AN 1998:184856 CAPLUS  
DN 128:293873  
TI Human **herpesvirus type 8 interleukin-6**  
homolog is functionally active on human myeloma cells  
SO Blood (1998), 91(6), 1858-1863  
CODEN: BLOOAW; ISSN: 0006-4971  
AU Burger, Renate; Neipel, Frank; **Fleckenstein, Bernhard**; Savino, Rocco; Ciliberto, Gennaro; Kalden, Joachim R.; Gramatzki, Martin  
AB Seroepidemiol. and polymerase chain reaction studies have strongly suggested that human **herpesvirus type 8** (**HHV-8**)

) is assocd. with Kaposi's sarcoma, Castleman's disease, and body cavity-based lymphoma. The genome of HHV-8 harbors a viral analog of the interleukin-6 (IL-6) gene. The amino acid sequence of the viral IL-6 (vIL-6) protein is 24.7% identical to human IL-6 (hIL-6). IL-6 as a B-cell growth and differentiation factor is known to play an essential role in the pathophysiol. of B-cell tumors. Thus, it seems possible that virus-encoded IL-6 contributes to malignant growth of HHV-8-pos. B-cell lymphatic tumors. We have tested a prepn. of HHV-8-derived IL-6 for the ability to promote the proliferation of the human myeloma cell line INA-6, which is strictly dependent on exogenous IL-6 for growth and survival. Viral IL-6 significantly induced DNA synthesis of INA-6 cells, but required much more protein on a wt. basis when compared with hIL-6 for maximal proliferation. The proliferative effect of vIL-6 was almost completely inhibited by a combination of anti-IL-6 receptor (IL-6R) and anti-gp130 antibodies or IL-6R superantagonist Sant7 and anti-gp130 antibodies. This report demonstrates that vIL-6 has proliferative activity on human cells and that the IL-6R and gp130 are involved in vIL-6 signaling in the myeloma cell line INA-6.

L18 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS

AN 1998:89360 CAPLUS

DN 128:166368

TI The interleukin 6 of human herpesvirus 8 and its use in diagnostics and therapeutics

SO PCT Int. Appl., 19 pp.

CODEN: PIXXD2

IN Fleckenstein, Bernhard; Albrecht, Jens-Christian; Neipel, Frank; Friedman-Kien, Alvin; Huang, Yao-Qi

AB Human herpesvirus 8 is found to carry a gene for an interleukin 6 that can bind to the interleukin 6 receptor. The interleukin and the gene encoding can be used in the diagnosis and treatment of a no. of diseases including: Kaposi sarcoma, Castleman's disease, multiple myeloma, kidney cell carcinoma, mesangial proliferative glomerulonephritis or B cell lymphoma. The protein may be manufd. by expression of the cloned gene.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9803657	A1	19980129	WO 1996-EP3199	19960719
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W: US

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 912742	A1	19990506	EP 1996-927558	19960719
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R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE

**Kaushal, Sumesh**

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**From:** Kaushal, Sumesh  
**Sent:** Friday, June 21, 2002 04:23 PM  
**To:** STIC-Biotech/ChemLib  
**Subject:** 09/230048 INTERFERENCE search

## **09/230048 INTERFERENCE search**

**Title:** VIRAL INTERLEUKIN-6  
**Inventor:** FLECKENSTEIN, BERNHARD

**SEQ ID NO: 1**  
**SEQ ID NO: 2**  
**SEQ ID NO: 2 (87-105)**

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